REMARKS

Reconsideration of this application is respectfully requested. Claims 1, 38 and 39 have been amended. With these amendments, claims 1, 4-7, 11-15, 18-22, 24-26, 28-30, and 32-39 are currently pending in this application. The specification has been amended. These amendments are made without prejudice or disclaimer and do not add any new matter. Applicants retain the right to prosecute any cancelled or otherwise unclaimed subject matter in a continuing, divisional or other application as appropriate. Consideration and entry of this reply is respectfully requested.

Claim Objections

Claim 37 refers to "between about 1.5 and 17 months after step (a)". Within claim 37, the term "1.5" means one point five, not fifteen (15). This is consistent with the administration schedule described in the specification at, for example, paragraph [0091]. Withdrawal of this objection is respectfully requested.

Rejection Under 35 U.S.C. § 112, second paragraph

(i) It is noted that the rejection of claims 18-22 under 35 U.S.C. § 112, second paragraph has been withdrawn. Applicants would like to clarify that the meaning of the phrase "through the course of that day" does not mean that administration needs to take place over the course of an entire day, and may refer to any suitable fraction of a day (e.g., a fraction of about a 24 hour period of time). Applicants believe this would be understood by one of skill in the art.

(ii) Claims 38 and 39 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants respectfully traverse these rejections as indicated below.

Claim 38 stands rejected as unclear because claim 1 recites "treating melanoma" while claim 38 recites "disease progression". Claim 38 has been amended to replace the term "disease" with "melanoma". Withdrawal of this rejection is therefore requested.

Claim 39 stands rejected as unclear as lacking antecedent basis for the term "the metastasis". Claim 38 has been amended to replace the phrase "the metastases" with

"melanoma metastases". Applicants believe this amendment addresses the rejection, and respectfully request withdrawal of the rejection.

It is noted that claim 1 has been amended to replace the term "host" with "mammal" (e.g., as in paragraph [0068] of the specification, "including humans and other mammals".

It is further noted that claim 1 relates to "[a] method for treating melanoma" which the skilled artisan would understand to mean that there was some evidence of melanoma progression before step (b) (e.g., the disease already exists in the mammal). Regarding claim 38, melanoma progression could be measured by any of a number of ways including (e.g., as shown in Applicants' Fig. 4). The skilled artisan would understand that it is standard practice to ascertain a base line or comparison from which the success of the treatment regimen is measured. As to claim 39 (now dependent upon claim 38), detection of metastases is a typical measure of melanoma progression as shown by Applicants in, for example, Fig. 4.

Rejection Under 35 U.S.C. § 112, first paragraph (new matter)

Claims 11 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not sufficiently described in the specification. The Office Action alleged that the incorporation by reference was ineffective, and that it would not be effective unless made to comply with 37 C.F.R. § 1.57(c). Paragraph [0018] has been amended to correct the citations referred to in the specification. The material now incorporated by reference is the material originally referred to in the specification. Applicants do not believe these corrections incorporate any new matter.

WO 98/14464 was one of two international patent applications that were cited by the Applicants as describing NY-ESO-1. Paragraph [0018] has been amended to insert reference to U.S. Pat. No. 6,274,145B1 (issued Aug. 14, 2001). The '145 patent describes NY-ESO-1 as being expressed in melanomas at, for example, Table 4 (col. 5, line 54) and col. 6, line 15.

U.S. Pat. No. 6,013,765, which the Office Action notes was properly incorporated by reference into Applicants' specification, was originally cited in the application as referring to the tumor antigen GAGE. Upon further review, it was noted that the '765

patent actually describes the DAGE antigen. Certain patent applications incorporated by reference into the '765 patent describe the tumor antigens BAGE and GAGE. These errors have been corrected with the amendment of paragraph [0018]. It is noted that expression of DAGE in melanoma primary lesions and metastases is shown at Table 2 of the '765 patent.

One of the patent applications incorporated by reference into the '765 patent is U.S. Ser. No. 08/079,110 which corresponds to U.S. Pat. No. 5,571,711 (issued Nov. 5, 1996). The '711 patent describes the BAGE antigen; paragraph [0018] of Applicants' specification has been amended accordingly. Expression of BAGE in melanomas is shown in Example 8, col. 6, line 34 of the '711 patent.

Similarly, the '765 patent also incorporates by reference U.S. Ser. No. 08/250,162 which corresponds to U.S. Pat. No. 5,610,013 (issued March 11, 1997). The '013 patent describes the GAGE antigen; paragraph [0018] of Applicants' specification has been amended accordingly. Expression of GAGE in melanomas is shown in Table 1 (col. 5, line 65) and Table 2 (col. 7, line 21) of the '013 patent.

As the specification has been amended in accordance with 37 C.F.R. § 1.57(c), it is therefore respectfully requested that these rejections be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Applicants understand that the references have been cited as a combination and are not attempting to argue against each reference individually outside of the combination. However, it is important to note the distinctions between what the Office Action alleged is taught by the individual references and what Applicants believe was actually disclosed in each in order to address the combination. Accordingly, while some of Applicants' remarks relate to each reference individually, this approach is necessary to show that the references, when combined as set out in the Office Action, cannot render the pending claims obvious.

A. Rejection of claims 1, 4-7, 11-15, 18-22, 28-30, 32-35 and 37-39 as obvious over Paoletti in view of Emtage, Kirkwood, and Aarts.

Claims 1, 4-7, 11, 12, 14, 15, 18-23 and 28-34 stand rejected as being unpatentable under 35 U.S.C. § 103(a) over Paoletti (U.S. Pat. No. 5,942,235) in view of Emtage (US 2003/0113919), Kirkwood (J. Clin. Oncol. 19(9): 2370-80 (2001)) and Aarts (Cancer Res. 62(20): 5770-7 (2002)). Applicants respectfully maintain that these rejections are inapplicable to the instantly pending claims.

The instantly pending claims relate to methods for inducing an anti-tumor immune response by first administering to a subject a nucleic acid-based vaccine "as the sole active pharmaceutical agent" (e.g., alone) and subsequently administering IFNα2b "as the sole active pharmaceutical agent" (e.g., alone). It is noted that claim 1 has been amended to replace the term "host" with "mammal". This method is exemplified by Applicants' Examples 1 and 2. As described therein, patients were vaccinated with an ALVAC vector encoding a tumor antigen and then treated with high dose IFNα2b. These patients demonstrated a robust anti-tumor immune response, including the elimination of systemic metastases (e.g., patients M166 and M335). Surprisingly, and in contrast to the teachings of the cited art, this was accomplished without simultaneously administering vaccine and cytokine. It is further noted that this was accomplished without additional vaccinations subsequent to administration of cytokine (e.g., as in claim 35). As described below, the cited art does not teach or suggest an immunization protocol that does not include simultaneous administration of vaccine and cytokine or repeated "boost" vaccinations following administration of cytokine.

As described in the Office Action, the previous rejection of claims 1, 11-13 and 24-26 as being unpatentable over Paoletti in view of Kirkwood and Aarts was withdrawn. The Office Actions states that the rejection was withdrawn because claim 1 was amended such that the compositions of steps (a) and (b) were each administered as the "sole active pharmaceutical agent". In this Office Action, Emtage is alleged to supplement the combination of Paoletti, Kirkwood, and Aarts by teaching "peptides, including tumor-associated antigen gp100…for use in diagnosing, treating, or preventing melanoma" and the use of "compositions of the invention…as the sole active pharmaceutical agent…."

Applicants respectfully disagree that this combination of references renders the instantly claimed method obvious.

The Office Action alleges that Aarts teaches "vector-based vaccine/cytokine combination therapy to enhance induction of immune responses to a self-antigen and anti-tumor activity", which relates to "subsequent[ly] administering a cytokine recited in step (b) of claim 1"). As previously pointed out, Applicants respectfully disagree with the characterization of Aarts of the previous Office Action, and maintain that position. However, as explained in the attached 37 C.F.R. § 1.131 declaration of inventor Dr. Neil Berinstein, the claimed method was actually reduced to practice by the inventors prior to the October 15, 2002 publication date of the reference. As explained by Dr. Berinstein in his declaration, he submitted a draft manuscript describing the claimed method (attached to his declaration as Appendix A) to his Sanofi Pasteur (at that time named Aventis Pasteur) patent attorney (the undersigned) on July 9, 2010. It is currently maintained as a file on the computer of the undersigned with the time / date of "Tuesday, July 09, 2002, 10:10:12 AM". Applicants maintain that the draft manuscript is evidence of actual reduction to practice prior to the earliest publication date of Aarts. Accordingly, the reference cannot be used in combination with Paoletti, Kirkwood, and Emtage to support a proper *prima facie* case of obviousness regarding the instantly pending claims. The Office Action does not indicate that any of Paoletti, Kirkwood, or Emtage may substitute for Aarts by providing the alleged teaching of vaccine/cytokine combination therapies. It is therefore respectfully requested that these rejections be withdrawn.

B. Rejection of claims 24-26 and 36 as obvious over Paoletti in view of Emtage, Kirkwood, Aarts, and Kawakami.

Claims 1, 4-7, 11, 12, 14, 15, 18-23 and 28-34 stand rejected as being unpatentable under 35 U.S.C. § 103(a) over Paoletti in view of Kirkwood, Emtage, Aarts as described in section (A) above, and further in view of Kawakami (U.S. Pat. No. 5,844,075). Applicants respectfully maintain that these references cannot be combined to support a *prima facie* case of obviousness against the instantly pending claims.

Applicants' position with respect to the combination of Paoletti, Kirkwood and Aarts were set forth in the preceding section, and are maintained with respect to these

rejections. In summary, Dr. Berinstein's 37 C.F.R. § 1.131 declaration demonstrates that Applicants' claimed invention was reduced to practice prior to Aarts' October 15, 2002 publication date. The Office Action alleges that Kawakami teaches gp100 peptides but does not suggest that the reference can substitute for Aarts' alleged teaching of vaccine/cytokine combination therapies. Accordingly, the reference cannot be used in combination with Paoletti, Emtage, and Kirkwood to support a proper *prima facie* case of obviousness regarding the instantly pending claims. It is therefore respectfully requested that these rejections be withdrawn.

CONCLUSIONS

Reconsideration of this application is respectfully requested. Applicants believe the claims are in condition for allowance and respectfully request the issuance of a Notice of Allowance as soon as possible. The Examiner is encouraged to contact the undersigned if it is believe doing so would expedite prosecution of this application.

Respectfully submitted,

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